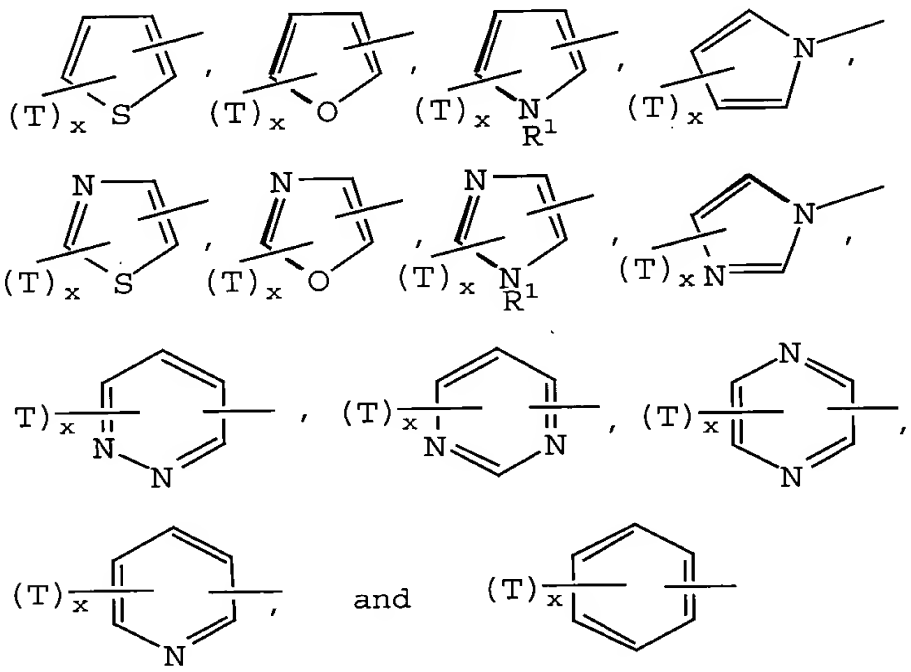
1. (Amended) A method of treating or preventing a respiratory disease, comprising administering to a mammal an effective amount of a compound having matrix metalloprotease inhibitory activity and the generalized formula:

$$(T)_xA\text{-}B\text{-}D\text{-}E\text{-}CO_2H$$

wherein

(a) $(T)_xA$ represents a substituted or unsubstituted aromatic or hetero-aromatic moiety selected from the group consisting of:



wherein R^1 represents H or alkyl of 1 - 3 carbons; and

each T represents a substituent group, independently selected from the group consisting of:

* the halogens -F, -Cl, -Br, and -I;
* alkyl of 1 - 10 carbons;
* haloalkyl of 1 - 10 carbons;

* haloalkoxy of 1 - 10 carbons;
* alkenyl of 2 - 10 carbons;
* alkynyl of 2 - 10 carbons;
* $-(CH_2)_pQ$, wherein
  p is 0 or an integer 1 - 4,
* -alkenyl-Q, wherein
  said alkenyl moiety comprises 2 - 4 carbons, and
* -alkynyl-Q , wherein
  said alkynyl moiety comprises 2 - 7 carbons; and

Q is selected from the group consisting of aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, -CN, -CHO, $-NO_2$, $-CO_2R^2$, $-OCOR^2$, $-SOR^3$, $-SO_2R^3$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-C(O)R^2$, $-N(R^4)_2$, $-N(R^2)COR^2$, $-N(R^2)CO_2R^3$, $-N(R^2)CON(R^4)_2$, $-CHN_4$, $-OR^4$, and $-SR^4$;

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wherein

R^2 represents H;
alkyl of 1 - 6 carbons;
aryl of 6 - 10 carbons;
heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or
arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or
heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R^3 represents alkyl of 1 - 4 carbons;
aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R^4 represents H;

alkyl of 1 - 12 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons;

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

alkenyl of 2 - 12 carbons;

alkynyl of 2 - 12 carbons;

$-(C_qH_{2q}O)_rR^5$ wherein q is 1-3; r is 1 - 3; and R^5 is H provided q is greater than 1, or alkyl of 1 - 4 carbons, or phenyl;

alkylenethio terminated with H, alkyl of 1-4 Carbons, or phenyl;

alkyleneamino terminated with H, alkyl of 1-4 carbons, or phenyl;

$-(CH_2)_sX$ wherein s is 1 - 3 and X is halogen;

$-C(O)OR^2$; or

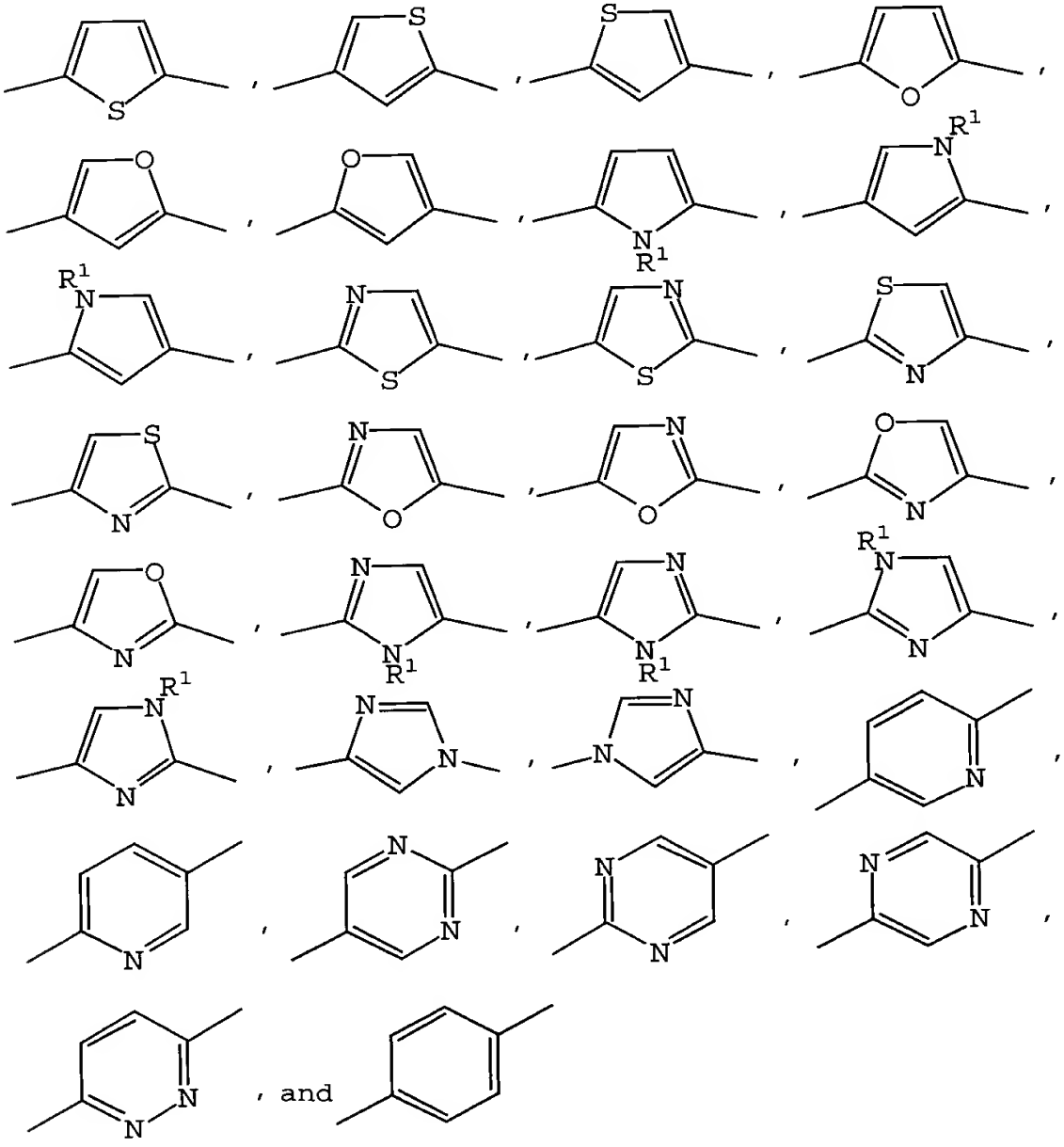
$-C(O)R^2$;

and with the provisos that a) when two R^4 groups are situated on a nitrogen, they may be joined by a bond to form a heterocycle, and b) unsaturation in a moiety which is attached to Q or which is part

of Q is separated from any N, O, or S of Q by at least one carbon atom, and

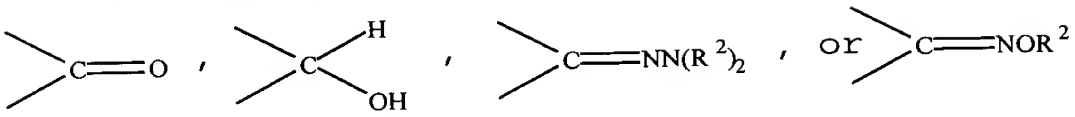
x is 0, 1, or 2;

(b) B represents a bond or an optionally substituted aromatic or hetero-aromatic ring containing 0-2 substituents T, which substituents T may independently have the meaning specified under (a), the B rings being selected from the group consisting of:



wherein R^1 is as defined above;

(c) D represents



in which R^2 is defined as above and each R^2 may be the same or different ;

(d) E represents a chain of n carbon atoms bearing m substituents R^6, wherein said R^6 groups are independent substituents, or constitute spiro or nonspiro rings in which a) two groups R^6 are joined, and taken together with the chain atom(s) to which said two R^6 group(s) are attached, and any intervening chain atoms, constitute a 3 - 7 membered ring, or b) one group R^6 is joined to the chain on which said one group R^6 resides, and taken together with the chain atom(s) to which said R^6 group is attached, and any intervening chain atoms, constitutes a 3 - 7 membered ring; and wherein

n is 2 or 3;

m is an integer of 1 - 3;

each group R^6 is independently selected from the group consisting of:

* fluorine;
* hydroxyl, with the proviso that a single carbon may bear no more than one hydroxyl substituent
* alkyl of 1 - 10 carbons;
* aryl of 6 - 10 carbons;
* heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;
* arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;

* heteroaryl-alkyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 8 carbons;
* alkenyl of 2 - 10 carbons;
* aryl-alkenyl wherein the aryl portion contains 6 - 10 carbons and the alkenyl portion contains 2 - 5 carbons;
* heteroaryl-alkenyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkenyl portion contains 2 -5 carbons;
* alkynyl of 2 - 10 carbons;
* aryl-alkynyl wherein the aryl portion contains 6 - 10 carbons and the alkynyl portion contains 2 - 5 carbons;
* heteroaryl-alkynyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkynyl portion contains 2 - 5 carbons;
* $-(CH_2)_tR^7$ wherein

t is 0 or an integer of 1 - 5; and

R^7 is selected from the group consisting of

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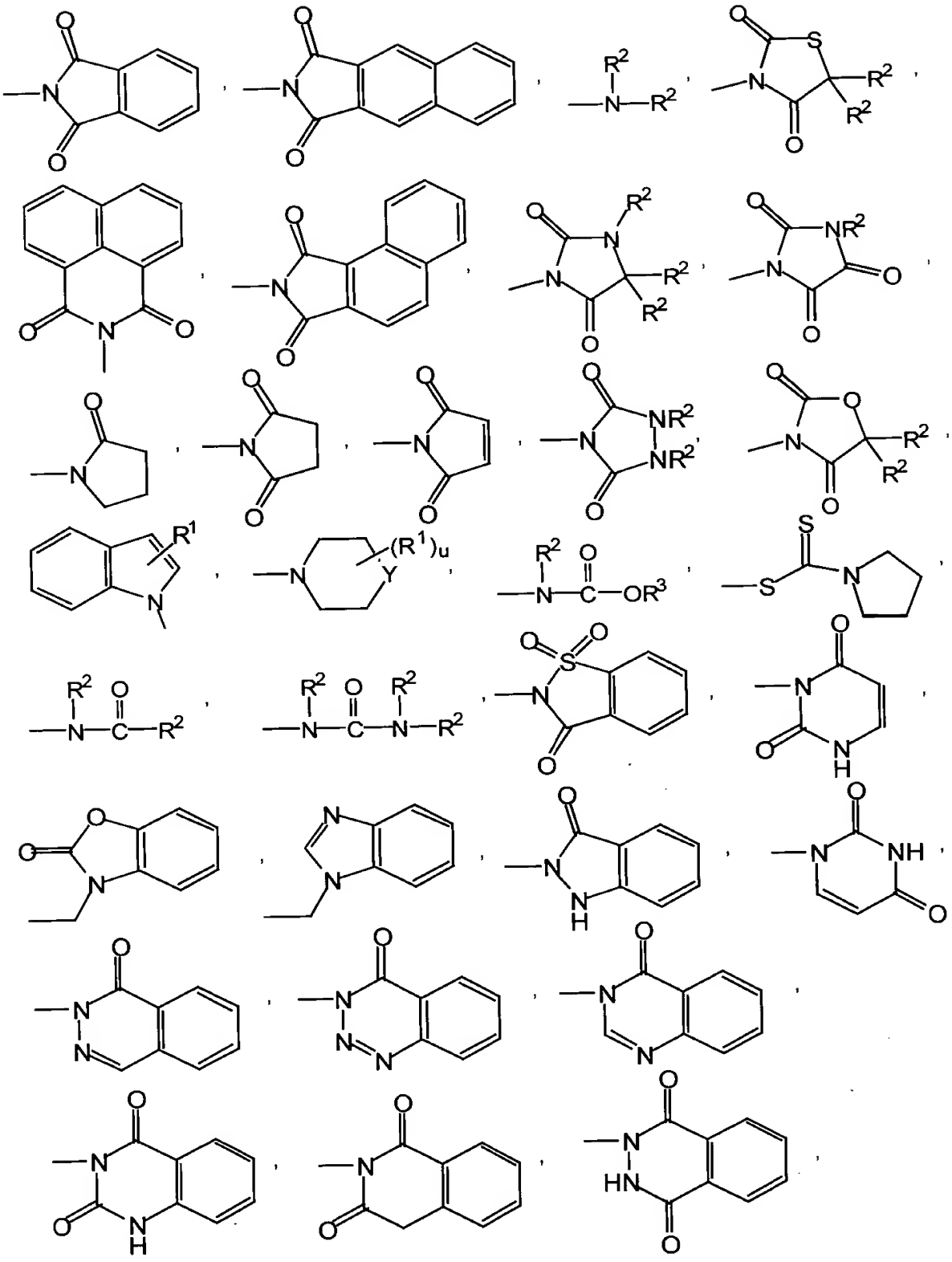


and corresponding heteroaryl moieties in which the aryl portion of an aryl-containing R^7 group comprises 4 - 9 carbons and at least one N, O, or S heteroatom;

wherein

Y represents O or S;

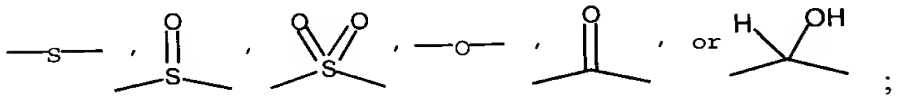
R^1, R^2, and R^3 are as defined above; and

u is 0, 1, or 2; and

* $-(CH_2)_vZR^8$ wherein

v is 0 or an integer of 1 to 4; and

Z represents



;

R^8 is selected from the group consisting of:

alkyl of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion contains 6 to 12 carbons and the alkyl portion contains 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$-C(O)R^9$ wherein R^9 represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion contains 6 - 10 carbons or is heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 4 carbons;

and with the provisos that

- when R^8 is $-C(O)R^9$, Z is S or O;
- when Z is O, R^8 may also be $-(C_qH_{2q}O)_rR^5$ wherein q, r, and R^5 are as defined above; and

* $-(CH_2)_wSiR^{10}{}_3$ wherein
  w is an integer of 1 to 3; and
  R^{10} represents alkyl of 1 to 2 carbons;

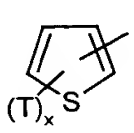
and with the proviso that

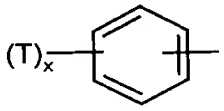
- aryl or heteroaryl portions of any of said T or R^6 groups optionally may bear up to two substituents selected from the group consisting of
$-(CH_2)_yC(R^4)(R^3)OH$, $-(CH_2)_yOR^4$, $-(CH_2)_ySR^4$, $-(CH_2)_yS(O)R^4$,
$-(CH_2)_yS(O)_2R^4$, $-(CH_2)_ySO_2N(R^4)_2$, $-(CH_2)_yN(R^4)_2$, $-(CH_2)_yN(R^4)COR^3$,
$-OC(R^4)_2O-$ in which both oxygen atoms are connected to the aryl ring,
$-(CH_2)_yCOR^4$, $-(CH_2)_yCON(R^4)_2$, $-(CH_2)_yCO_2R^4$, $-(CH_2)_yOCOR^4$,
-halogen, -CHO, $-CF_3$, $-NO_2$, -CN, and $-R^3$, wherein
  y is 0 - 4; and
  R^3 and R^4 are defined as above; and any two R^4 which are attached to one nitrogen may be joined to form a heterocycle;

and pharmaceutically acceptable salts and prodrugs thereof.

2. (Amended) The method of claim 1, wherein

(a) $(T)_xA$ represents a substituted or unsubstituted aromatic or hetero-aromatic moiety selected from the group consisting of:



and


wherein

each T represents a substituent group, independently selected from the group consisting of:

* the halogens -F, -Cl, -Br, and -I;
* alkyl of 1 - 10 carbons;
* haloalkyl of 1 - 10 carbons;
* alkenyl of 2 - 10 carbons;
* alkynyl of 2 - 10 carbons;
* $-(CH_2)_pQ$, wherein
  p is 0 or an integer 1 - 4,
* -alkenyl-Q, wherein
  said alkenyl moiety comprises 2 - 4 carbons, and
* -alkynyl-Q , wherein
  said alkynyl moiety comprises 2 - 7 carbons; and

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Q is selected from the group consisting of $-OR^4$ and $-SR^4$;

wherein

R^4 represents H;

alkyl of 1 - 12 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons;

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$-C(O)OR^2$; or

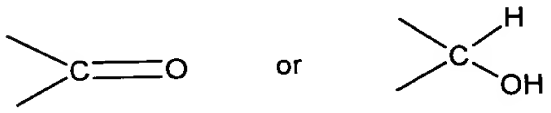
$-C(O)R^2$;

and with the proviso that unsaturation in a moiety which is attached to Q or which is part of Q is separated from any N, O, or S of Q by at least one carbon atom, and

x is 0, 1, or 2;

(b) B represents an optionally substituted phenyl or thienyl ring containing 0-2 substituents T, which substituents T may independently have the meaning specified under (a).

(c) D represents



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(d) E represents a chain of n carbon atoms bearing m substituents R^6, wherein said R^6 groups are independent substituents, or constitute nonspiro rings in which two groups R^6 are joined, and taken together with the chain atom(s) to which said two R^6 group(s) are attached, and any intervening chain atoms, constitute a 5 or 6- membered ring; and wherein

n is 2 or 3;

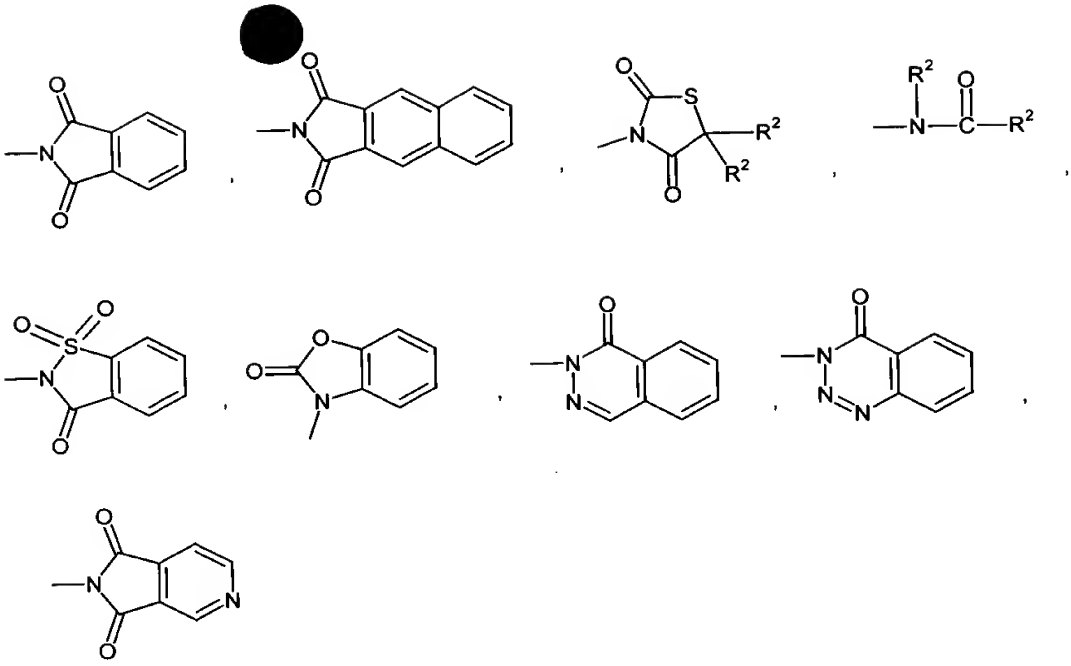
m is an integer of 1 or 2;

each group R^6 is independently selected from the group consisting of:

* arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;
* $-(CH_2)_tR^7$ wherein

  t is 0 or an integer of 1 - 5; and

  R^7 is selected from the group consisting of



wherein

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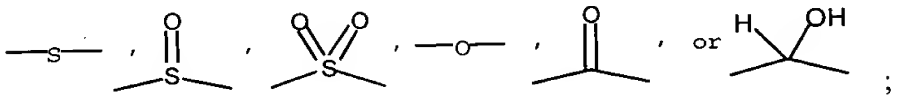
R^2 is independently selected from the group consisting of: H; aryl of 6-10 carbons

* $-(CH_2)_vZR^8$ wherein

v is 0 or an integer of 1 to 4; and

Z represents



;

R^8 is selected from the group consisting of:

alkyl of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion contains 6 to 12 carbons and the alkyl portion contains 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$-C(O)R^9$ wherein R^9 represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion contains 6 - 10 carbons or is heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 4 carbons;

and with the provisos that

- when R^8 is $-C(O)R^9$, Z is S or O;
- when Z is O, R^8 may also be $-(C_qH_{2q}O)_rR^5$ wherein q, r, and R^5 are as defined above; and

* $-(CH_2)_wSiR^{10}{}_3$ wherein
  w is an integer of 1 to 3; and
  R^{10} represents alkyl of 1 to 2 carbons;

and with the proviso that

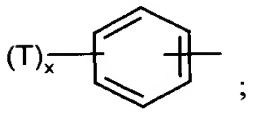
- aryl or heteroaryl portions of any of said T or R^6 groups optionally may bear up to two substituents selected from the group consisting of OR^4, $N(R^4)_2$, $-OC(R^4)_2O-$ in which both oxygen atoms are connected to the aryl ring, $CON(R^4)2$, $OCOR^4$, -halogen, $-NO_2$, and alkyl with up to 6 carbon atome wherein
  R^4 is defined as above;

and pharmaceutically acceptable salts and prodrugs thereof.

3. (Amended) The method of claim 1 or 2, wherein at least one of the units A, B, T, and R^6 comprises a heteroaromatic ring.

4. (Amended) The method of claim 1or 2, wherein in said B unit, n is 2 and m is 1.

5. (Amended) The method of claim 1or 2, wherein A is



;

B is p-phenylene and D is a carbonyl group.

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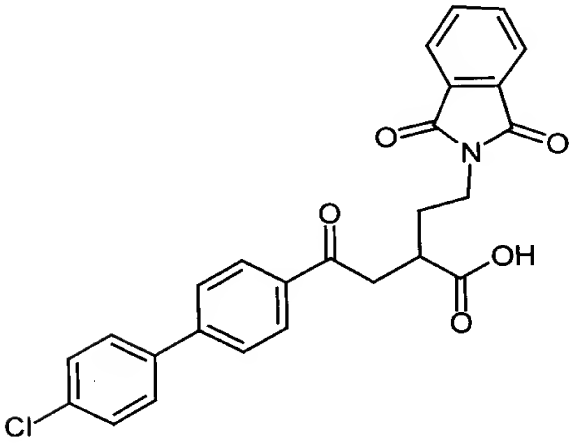
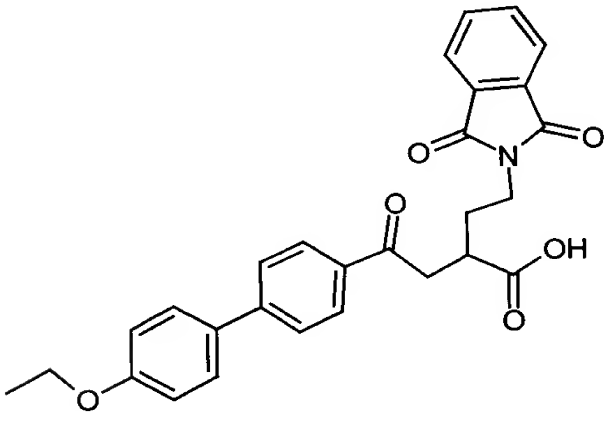
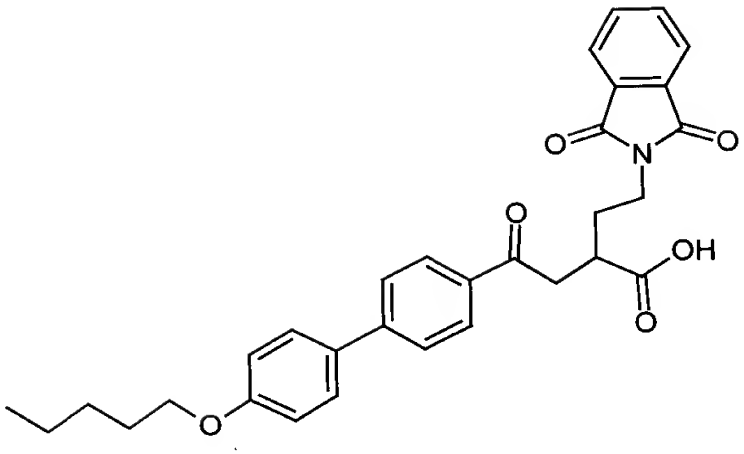
6. (Amended) The method of claim 1 or 2, wherein the compound is selected from the following group:







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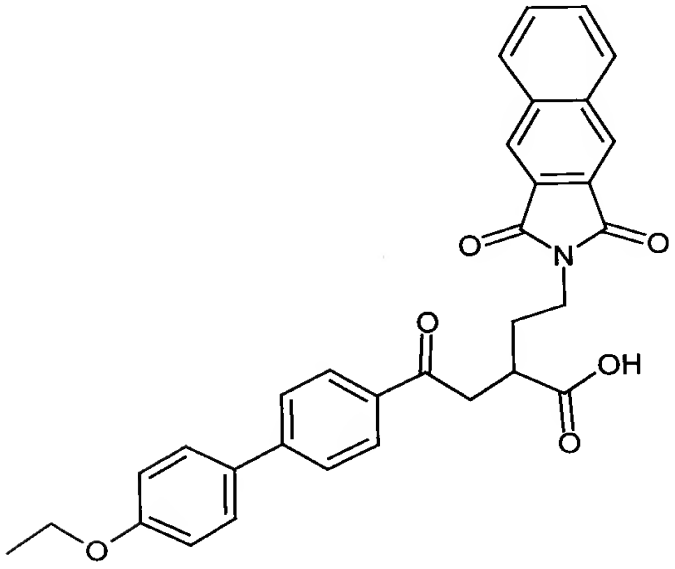

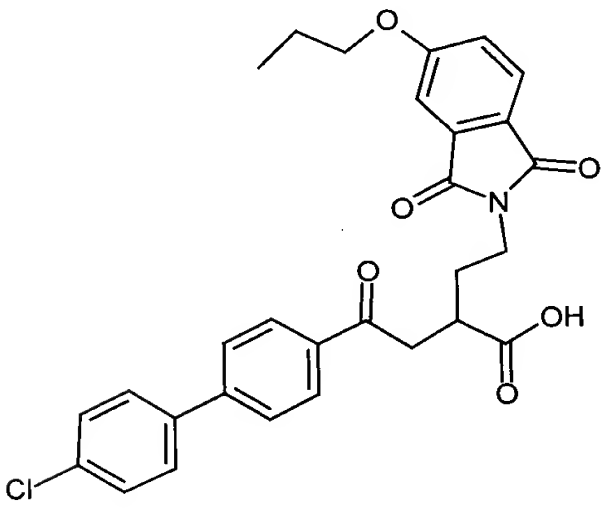

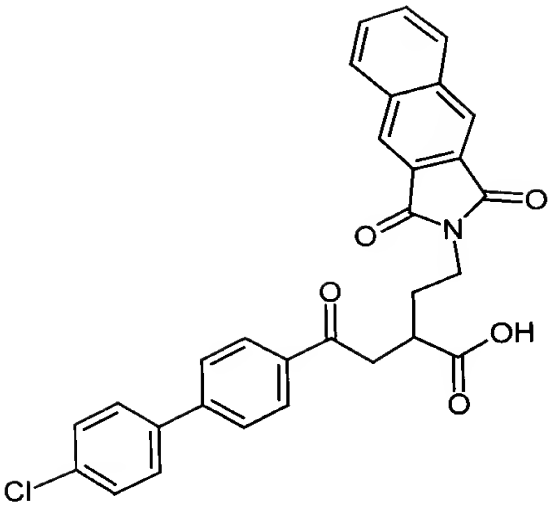

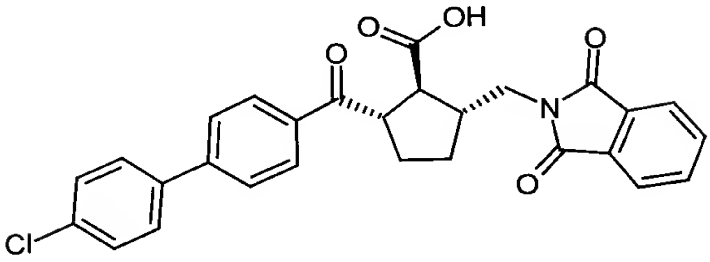

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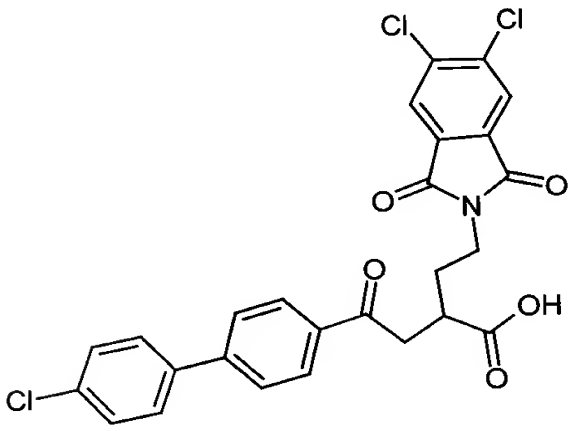

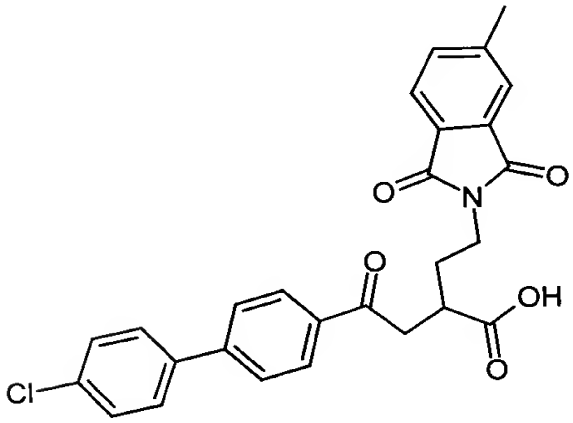

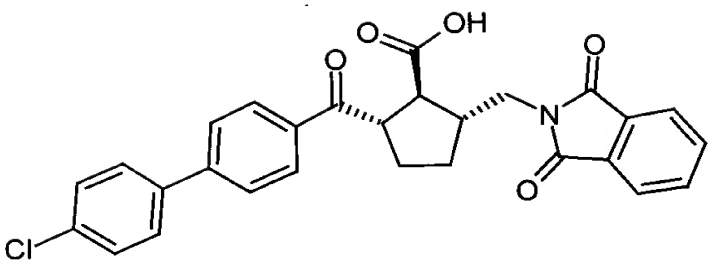

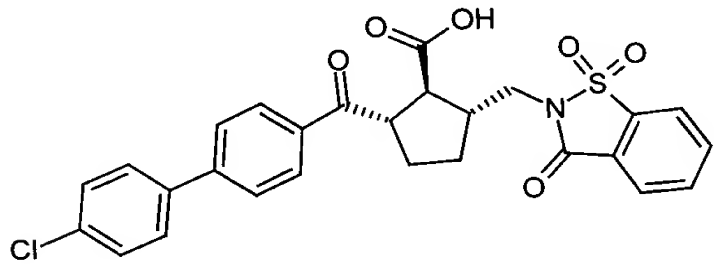

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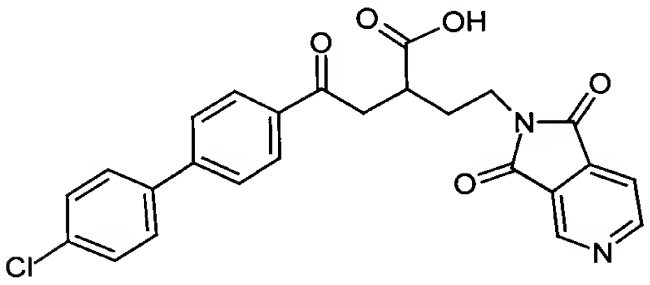

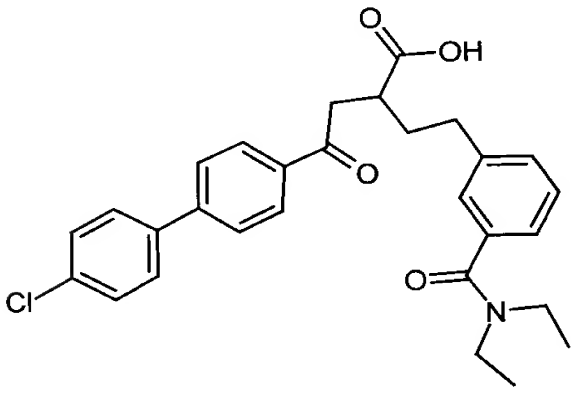

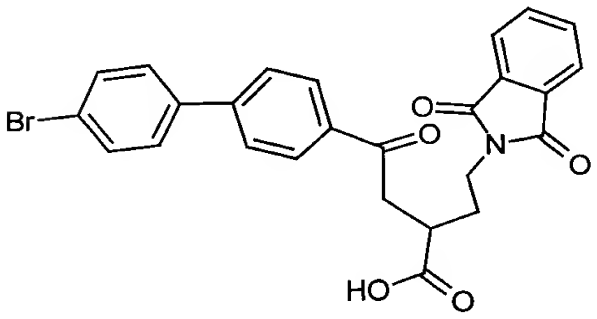

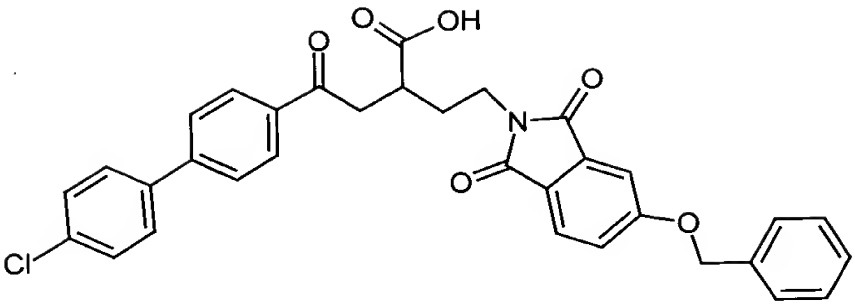

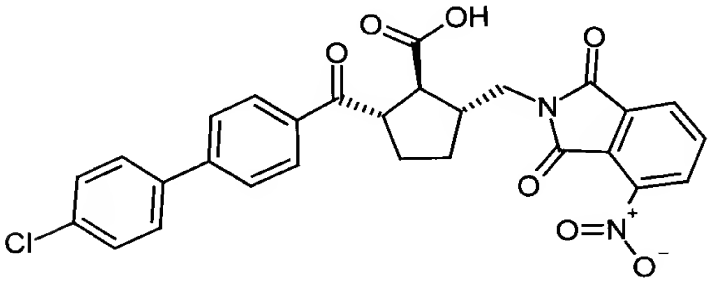

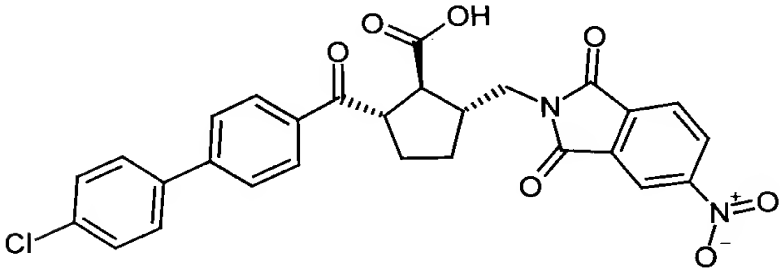

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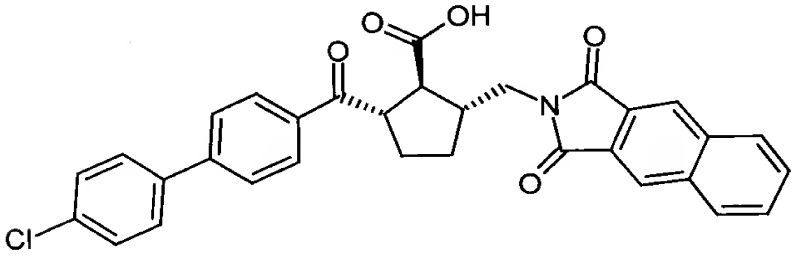

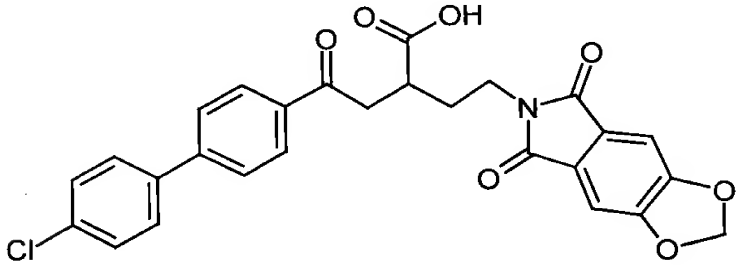

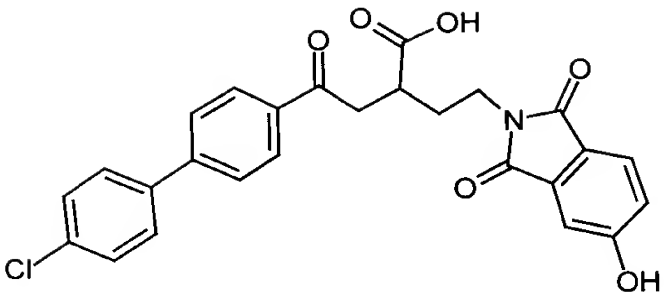

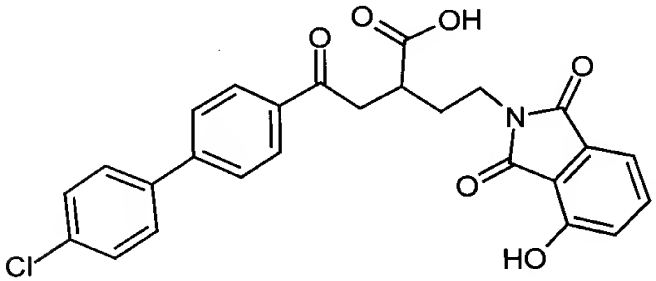

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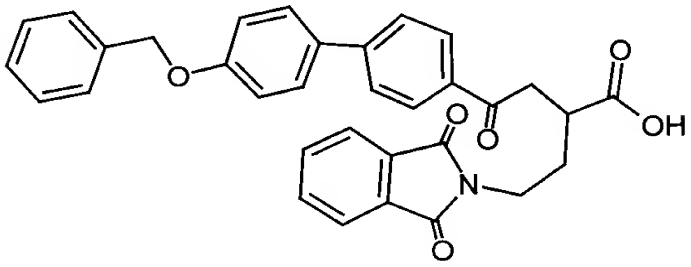

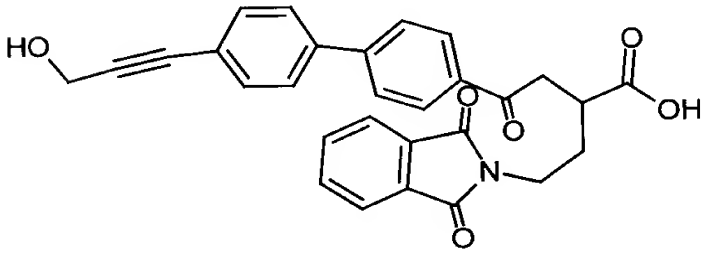

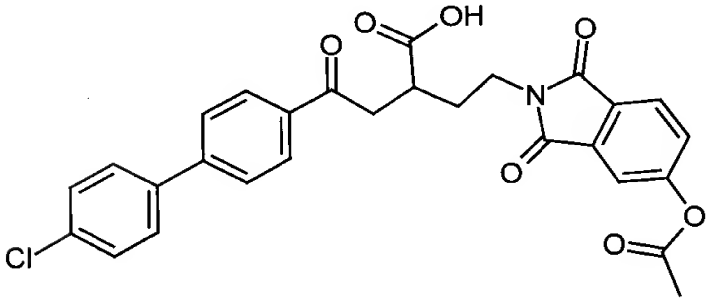

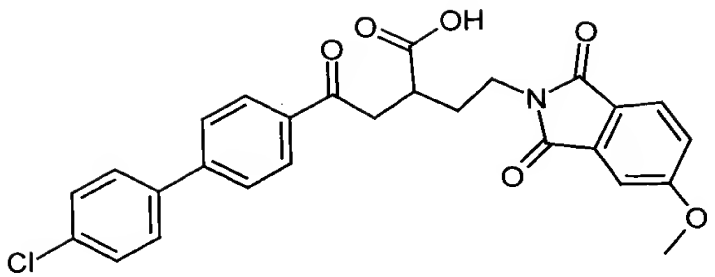

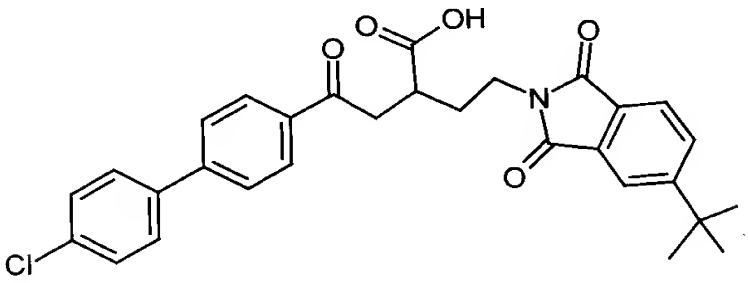

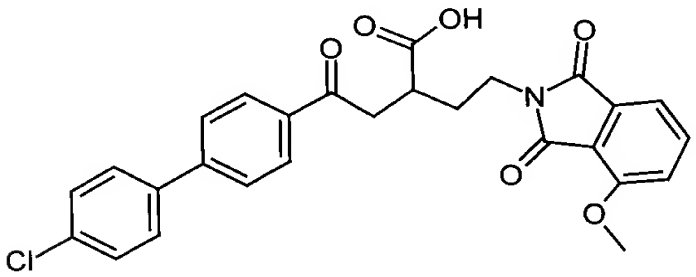

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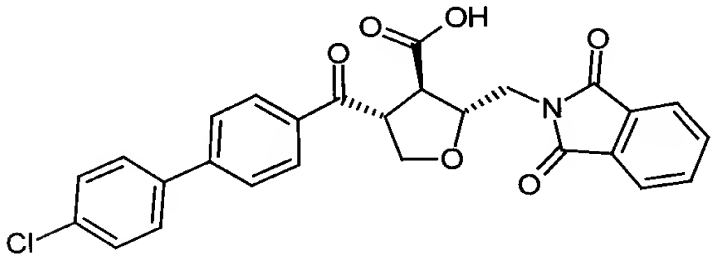
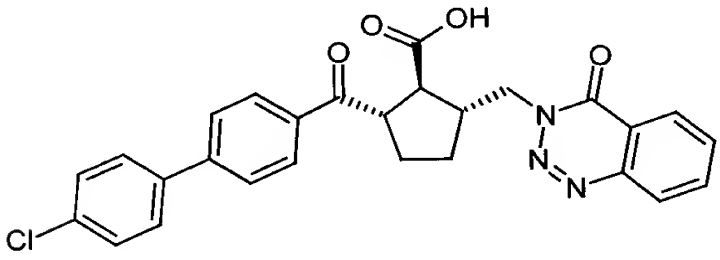
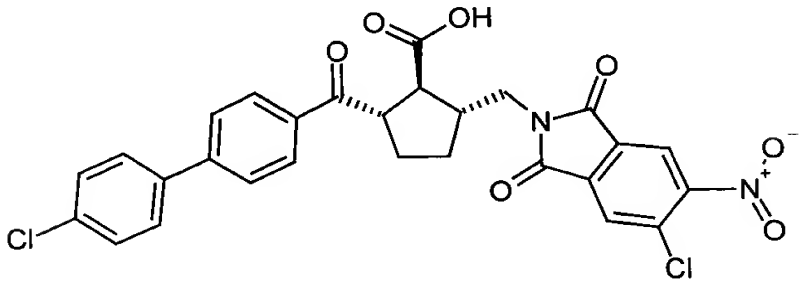
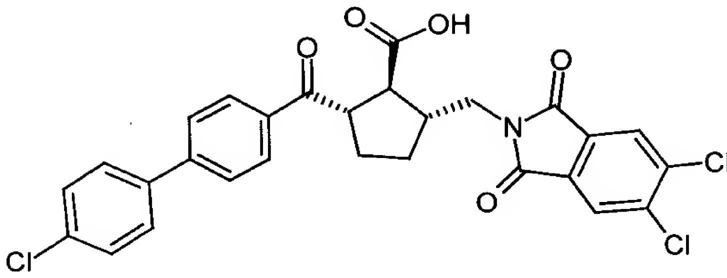
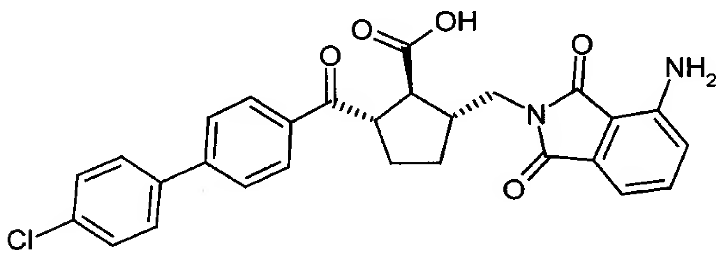
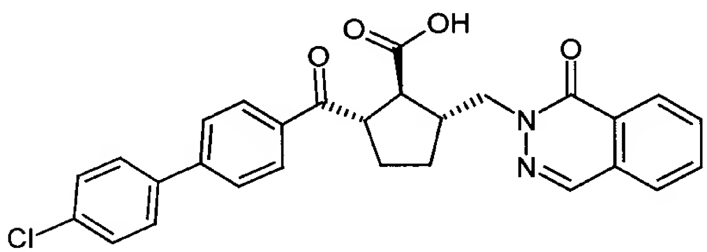


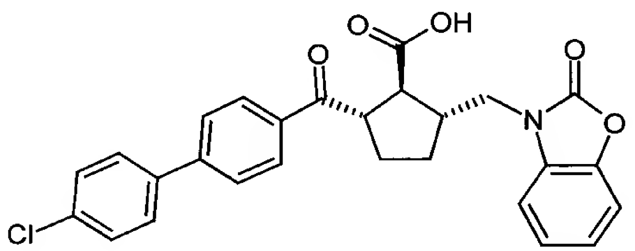


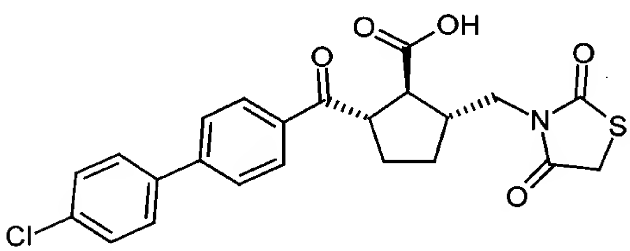


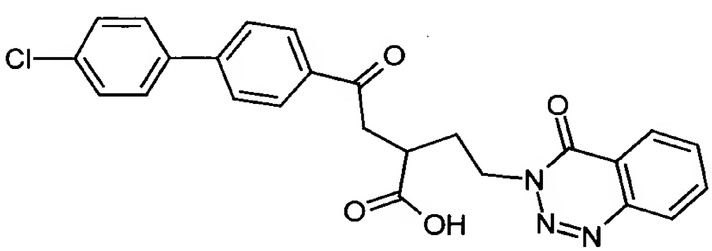




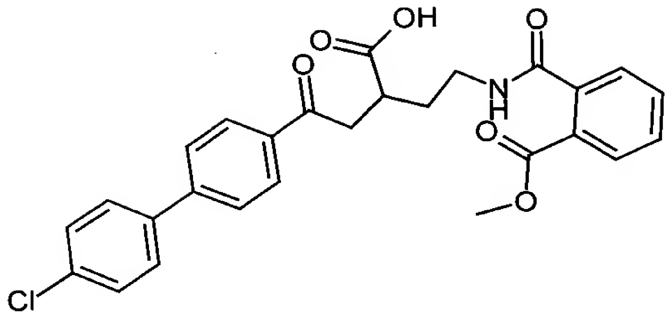


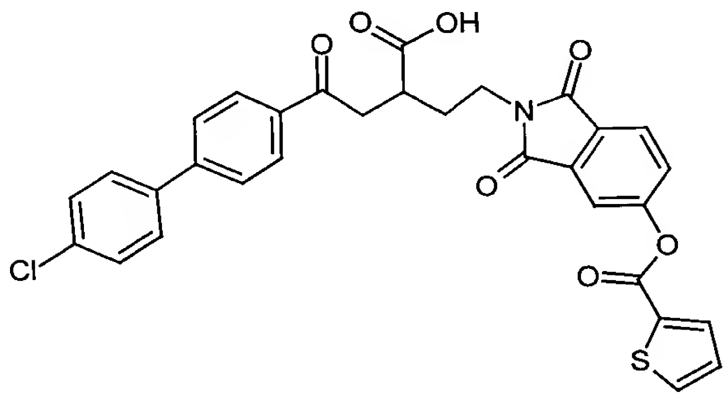


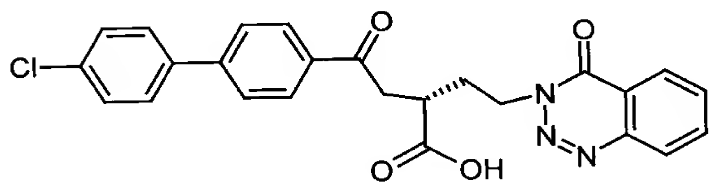




A¹

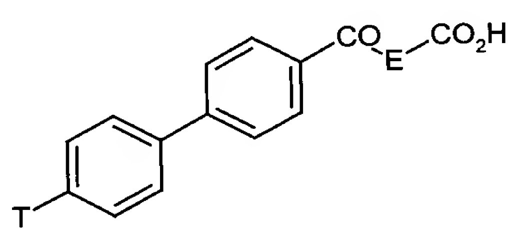






A²

9. (Amended) A method of treating or preventing a respiratory disease, comprising administering to a mammal an effective amount of a compound of the general formula (I')



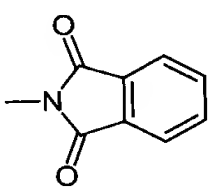
(I')

wherein

T is (C_1-C_4)-alkoxy, chloride, bromide, fluoride, acetoxy, hydroxy, cyano, trifluoromethyl or trifluoromethoxy,

$CO\text{-}E\text{-}CO_2H$ represents a 3-carboxyl-5-R^7-pentan-1-on-1-yl- or a 2-carboxyl-3-(R^7-methyl)-cyclopentan-1-yl)carbonyl-residue, and

R^7 represents a group of the formula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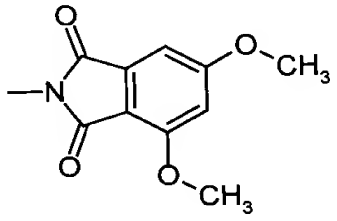
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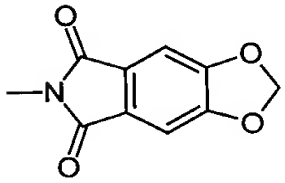
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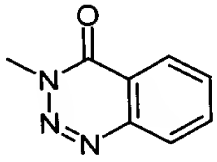
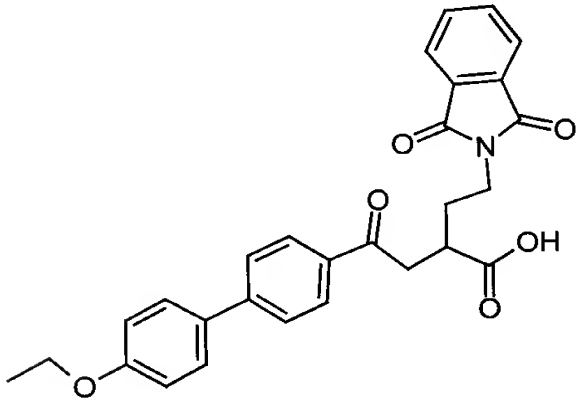
or


and their salts.

A2

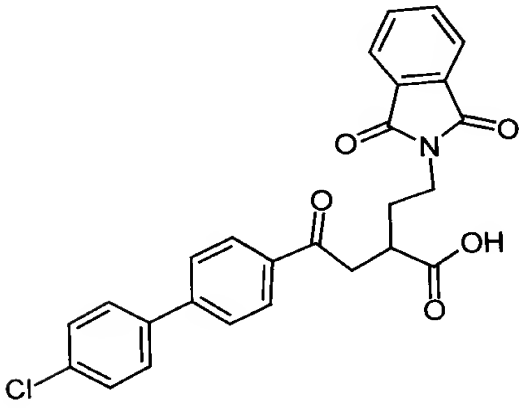
10. (Amended) A method of treating or preventing a respiratory disease, comprising administering to a mammal an effective amount of the compound (+)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-(4'-ethoxy[1,1'-biphenyl]-4-yl)-4-oxobutanoic acid,



11. (Amended) A method of treating or preventing a respiratory disease, comprising administering to a mammal an effective amount of the compound

(+)-4-(4'-chloro[1,1'-biphenyl]-4-yl)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-oxobutanoic acid

A2



12. canceled.

14. The method of claim 1, 9, 10 or 11, wherein said respiratory disease is selected from the group consisting of asthma; chronic obstructive pulmonary diseases including chronic bronchitis and emphysema; cystic fibrosis; bronchiectasis; adult respiratory distress syndrome (ARDS); allergic respiratory disease including allergic rhinitis; diseases linked to TNF_{α} production including acute pulmonary fibrotic diseases, pulmonary sarcoidosis, silicosis, coal worker's pneumoconiosis, alveolar injury in mammals, such as human, a farm animal or a domestic pet.

A3

15. canceled.

16. (Amended) A pharmaceutical composition comprising a compound according to Claim 7 or 8 and a pharmaceutically acceptable carrier.

A4

17. (Amended) A method of treating or preventing acute and chronic inflammatory processes, comprising administering to a mammal an effective amount of a compound according to claim 7 or 8.